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TEMPLATE:

MBFi LLC

3F9084

EPA has received a pesticide petition (3F9084) from MBFi LLC (11125 North Ambassador Drive, Suite 120, Kansas City, MO 64153) requesting, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 to establish an exemption from the requirement of a tolerance for the microbial pesticide *Trichoderma asperellum* DSM336496 in or on all food and feed commodities.

Pursuant to section 408(d)(2)(A)(i) of FFDCA, as amended, MBFi LLC has submitted the following summary of information, data, and arguments in support of their pesticide petition. This summary was prepared by MBFi LLC and EPA has not fully evaluated the merits of the pesticide petition. The summary may have been edited by EPA if the terminology used was unclear, the summary contained extraneous material, or the summary unintentionally made the reader conclude that the findings reflected EPA's position and not the position of the petitioner.

I. MBFi LLC Petition Summary

3F9084

A. Product Name and Proposed Use Practices

Trichoderma asperellum DSM33649 is used for the control of soil-borne diseases on various agricultural and greenhouse crops, as well as terrestrial and indoor ornamental plants and turf.

B. Product Identity/Chemistry

1. *Identity of the pesticide and corresponding residues.* *Trichoderma asperellum* DSM33649

2. *Magnitude of residues at the time of harvest and method used to determine the residue.* MBFi LLC is requesting an exemption from the requirement of a tolerance for residues of *Trichoderma asperellum* DSM33649; therefore, the requirement to provide residue data and an analytical method for the detection of *Trichoderma asperellum* DSM33649 in agricultural commodities or processed foods is not applicable.

3. *A statement of why an analytical method of detecting and measuring the levels of the pesticide residue are not needed.* MBFi LLC is requesting an exemption from the requirement of a tolerance for residues of *Trichoderma asperellum* DSM33649; therefore, the requirement to provide residue data and an analytical method for the detection of *Trichoderma asperellum* DSM33649 in agricultural commodities or processed foods is not applicable.

C. Mammalian Toxicological Profile

Acute Intraperitoneal Toxicity/Pathogenicity (OCSPP 885.3200)

A study was conducted to evaluate the acute intraperitoneal toxicity and infectivity of *T. asperellum* DSM33649 in 13 male and 17 female Sprague-Dawley rats. *T. asperellum* DSM33649 was administered to rats intraperitoneally in a single dose of $>10^7$ CFU/rat and rats were given an adequate post-exposure observation period. One untreated control female and three test item-treated females were used in Experiment III for confirmatory reasons, as Day 21 females of Experiment II were not injected properly (abscesses were found in the skin). The animals were observed frequently on the day of dosing for mortality and signs of pharmacologic and/or toxicologic effects and once daily thereafter for 21 days. An untreated control group and a group treated with inactivated test substance were conducted concurrently.

There was no mortality during the study. There were no signs of pharmacologic and/or toxicologic effects observed in any of the animals during the study. The gross necropsy conducted at termination of the study revealed no internal or external observable abnormalities.

The test organism was not seen in the brain tissue at any time and appeared to be clear from the blood and the kidneys by Day 21. The test organism showed a pattern of clearance from the lungs, liver, mesenteric lymph nodes, and cecum contents of the activated *T. asperellum* DSM33649 TGAI group.

The test substance was determined to be non-toxic, non-infective, and non-pathogenic to rats when administered by intraperitoneal injection in a single dose of $>10^7$ CFU/rat.

Acute Pulmonary Toxicity/Pathogenicity (OCSPP 885.3150)

In a study to evaluate the pulmonary toxicity, infectivity, and pathogenicity, *T. asperellum* DSM33649 was administered to rats by intratracheal injection in a single dose of approximately >2.0 x 10^7 CFU/rat and rats were given an adequate post-exposure observation period. A control group (untreated) was conducted concurrently. The animals were observed frequently on the day of dosing for mortality and signs of pharmacologic and/or toxicologic effects, and once daily thereafter for 42 or 84 days, as applicable. Tissue and blood samples taken at interim sacrifices from the group receiving the active test substance were cultured to provide quantitative measurements of the test microbe's clearance pattern.

There were no signs of pharmacologic and/or toxicologic effects observed in any animal during the study, with the exception of transient noisy respiration observed for some animals within the first hour after test item administration. The gross necropsy conducted at termination of the study revealed discoloration of lung and enlarged mediastinal lymph nodes. In some cases, foci of the lung and/or enlarged lung lobes were also observed.

The test organism was not seen at any time in the treated animal group's blood, kidneys, mesenteric lymph nodes, brain, liver, spleen, and cecum contents. The test substance was seen in the lungs on Days 0, 3, 7, 14, 21, and 42. Clearance was established by Day 84.

The test substance, *T. asperellum* DSM33649, was determined to be non-toxic, noninfective, and non-pathogenic to rats when administered by intratracheal injection in a single dose of approximately >2.0 x 10^7 CFU/rat.

Acute Oral Toxicity (OCSPP 870.1100)

In a study to evaluate the acute oral toxicity of *T. asperellum* DSM33649 was administered to female rats by gavage in a single high-dose exposure of 5000 mg/kg and rats were given an adequate post-exposure observation period. The animals were observed frequently on the day of dosing for mortality and signs of toxicologic effects and once daily thereafter for 14 days.

There was no mortality during the study. Clinical signs in one animal included piloerection on Day 1 and dark feces on Days 4 and 5.

The gross necropsy conducted at termination of the study revealed no internal or external observable abnormalities.

The test substance, *T. asperellum* DSM33649, was determined to be non-toxic to rats when administered by oral gavage in a single dose of 5000 mg/kg. The LD50 was determined to be greater than 5000 mg/kg.

Acute Dermal Toxicity (OCSPP 870.1200)

In a study to evaluate the acute dermal toxicity, *T. asperellum* DSM33649 was applied to rats on an exposed area of skin in a single high dose exposure of 2020 mg/kg for 24 hours. Rats were given an adequate post-exposure observation period. The animals were observed frequently on the day of dosing for mortality and signs of toxicologic effects and once daily thereafter for 14 days.

There was no mortality during the study. There were no signs of toxicologic effects or dermal irritation observed in any of the animals during the study.

The gross necropsy conducted at termination of the study revealed no internal or external observable abnormalities.

T. asperellum DSM33649 was determined to be non-toxic to rats when applied directly to skin in a single dose of 2020 mg/kg (the highest dose tested). The LD50 was determined to be greater than 2020 mg/kg.

Acute Inhalation Toxicity (OCSPP 870.1300)

In a study to evaluate the acute inhalation toxicity, *T. asperellum* DSM33649 was administered to rats via aerosol exposure of 2.05 mg/L for four hours. Rats were given an adequate post-exposure observation period. The animals were observed frequently on the day of dosing for mortality and signs of toxicologic effects and once daily thereafter for 14 days.

There was no mortality during the study. There were no signs of toxicologic effects or adverse effects observed in any of the animals during the study.

The gross necropsy conducted at termination of the study revealed no internal or external observable abnormalities, with the exception of mottled lungs in all animals.

The test substance, *T. asperellum* DSM33649, was determined to be non-toxic to rats when administered by aerosol in a single dose of 2.05 mg/L . The LC50 was determined to be greater than 2.05 mg/L.

Primary Eye Irritation (OSCPP 870.2400)

In an eye irritation study, 100 mg of *T. asperellum* DSM33649, containing 1.36 x 10^{10} CFU/g, was instilled into one eye of each of three adult male rabbits. Observations were made 1, 24, 48, and 72 hours after instillation, and at 4, 7, 10 and 14 days after treatment. Exposure to the test item resulted in positive effects in all test-item animals. The corneae, irises, and conjunctivae were positively affected by instillation of the test item, but cleared by Day 14. Therefore, *T. asperellum* DSM33649 was considered to be moderately irritating to the eyes of rabbits.

Primary Dermal Irritation (OSCPP 870.2500)

In a primary dermal irritation study, three adult female rabbits were exposed dermally to 500 mg of *T. asperellum* DSM33649 which contained 1.36 x 10^{10} CFU/g. The test material was applied for four hours to the clipped skin of one flank of each animal and held in place with semi-occlusive dressing. Observations were made 1, 24, 48, and 72 hours after exposure. No erythema or edema was observed at any time throughout the study. No clinical signs were observed two hours after patch removal. No symptoms of systemic toxicity were observed and no mortality occurred. Therefore, *T. asperellum* DSM33649 was considered to be non-irritating to the skin of rabbits.

Hypersensitivity Incidents

No reports of hypersensitivity have been associated with *Trichoderma asperellum DSM33649*.

D. Aggregate Exposure

1. *Dietary exposure.* Dietary exposure to this active ingredient is possible through application of treated crops. *T. asperellum* DSM33649 is naturally occurring and is not toxic or pathogenic. Therefore, exposure to any residues of T. asperellum DSM33649 from food should not be of concern for human health.

i. *Food.* There are no current pesticide uses of *Trichoderma asperellum DSM33649*; therefore, exposure to *T. asperellum* DSM33649 will be limited to occurrence through consumption of treated agricultural crops. *T. asperellum* DSM33649 is naturally-occurring and is not toxic or pathogenic. Therefore, exposure to any residues of *T. asperellum* DSM33649 from food should not be of concern for human health.

ii. *Drinking water. Trichoderma asperellum* DSM33649 will not be applied directly to water. Runoff from field applications could occur; however, *T. asperellum* DSM33649 is naturally-occurring and is not toxic or pathogenic. Therefore, exposure to any residues of *T. asperellum* DSM33649 from drinking water should not be of concern for human health.

2. *Non-dietary exposure*. The potential for non-dietary exposure to *T. asperellum* DSM33649 to the general population is possible when the end-use products, Trillum DS and Trillum WP, are used on greenhouse and terrestrial agricultural crops, terrestrial and indoor ornamental plants, and turf. Personal protective equipment mitigates the potential for exposure to applicators and handlers of *T. asperellum* DSM33649 when used in

agricultural settings. *T. asperellum* DSM33649 is naturally-occurring and is not toxic or pathogenic. Therefore, non-dietary exposure to any residues of *T. asperellum* DSM33649 should not be of concern for human health.

E. Cumulative Effects

Other *Trichoderma* species are used as active ingredients in registered pesticide products. However, cumulative adverse effects via a common mechanism of toxicity are not anticipated based on the lack of toxicity/pathogenicity of *Trichoderma asperellum* DSM33649.

F. Safety Determination

1. *U.S. population. T. asperellum* DSM33649 is naturally-occurring and is not toxic or pathogenic; therefore, exposure to any residues of *T. asperellum* DSM33649 should not be of concern for human health.

2. *Infants and children*. As mentioned above, *T. asperellum* DSM33649 is naturally-occurring and is not toxic or pathogenic; therefore, exposure to *T. asperellum* DSM33649 should not be of concern for human health nor should infants and children be at an increased risk

G. Effects on the Immune and Endocrine Systems

There is no evidence to suggest *Trichoderma asperellum* DSM33649 functions in a manner similar to any known hormone or that it acts as an endocrine disrupter.

H. Existing Tolerances

There are no existing tolerances for *Trichoderma asperellum* DSM33649. There are, however, established tolerance exemptions for nine other *Trichoderma* species and strains, including three *T. asperellum* strains:

- § 180.1102 *Trichoderma harzianum* KRL-AG2 (ATCC #20847) strain T-22; exemption from requirement of a tolerance.
- § 180.1293 *Trichoderma gamsii* strain ICC 080; exemption from the requirement of a tolerance.
- § 180.1294 *Trichoderma asperellum* strain ICC 012; exemption from the requirement of a tolerance.
- § 180.1298 *Trichoderma hamatum* isolate 382; exemption from the requirement of a tolerance.
- § 180.1310 *Trichoderma virens* strain G-41; exemption from the requirement of a tolerance.
- § 180.1331 *Trichoderma asperelloides* strain JM41R; exemption from the requirement of a tolerance.
- § 180.1378 *Trichoderma atroviride* strain SC1; exemption from the requirement

of a tolerance.

- § 180.1379 *Trichoderma asperellum* strain T34; exemption from the requirement of a tolerance.
- § 180.1390 *Trichoderma harzianum* strain T-78; exemption from the requirement of a tolerance.

I. International Tolerances

No international tolerances are known for *Trichoderma asperellum* DSM33649.